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Dear Josh,

Sorry that I haven't answered your letter before this, but I have been trying to decide exactly what I want to do. A good many of the mutants for which I asked you have been isolated by us. We have the Cst + Gal - by recombination, as well as the melibiose negative, arabinose negative, and other galactose negative mutants. The only lac - mutants of K 12 that we have, are the Lac_1-. I should like to have the whole series of lac - mutants. I don't want to put you to a great deal of trouble, as it will be several months before I can take up this problem again. I am in the process of preparing good antisera.

I thought you might be interested in knowing what we're up to these days. We have been looking into a phenomenon which we call "specific inhibition". On the assumption that constitutive enzymes are constitutive only because their inducers are spontaneously synthesized intermediates in cell metabolism, we tried to see whether analogues of supposed inducers would inhibit constitutive enzyme synthesis. One of the most obvious analogues is the product of enzyme action. We uncovered three systems which worked beautifully. The constitutive β-galactosidase is inhibited by galactose; the tryptophane desmolase by tryptophane, and the methionine - synthase (enzyme converting homocysteine to methionine) by methionine. These three cases are extremely encouraging, and I don't think it will be too long before we have proof of the hypothesis.

The mechanism of the diauxie has been clarified. Glucose inhibits induction of β galactosidase, not by competing for precursors, but by blocking one of the early steps (probably the penetration) of inducer metabolism. This can be shown by treating concentrated non-growing cell suspensions with an inducer and then diluting them out into glucose, so that external inducer can no longer act. There is synthesis of the enzyme, which follows a hyperbolic curve.

We have started work on three new enzymes, the α-galactosidase of K 12, a β glucosidase of yeast, and a glucose-oxidase of neisseria. So far, we have nothing but confirmation of what we have found with β galactosidase.

The isotope work to see whether there are any precursors of galactosidase, is coming along painfully, but we are now at the stage where the enzyme can be isolated from other cellular proteins. We hope to have the answers in a few months.

Wonder whether you will be coming to the International Congress in Rome this year.

Yours sincerely,

Mel

Enjoyed tremendously your paper with Zinder on transduction.